Mod Rheumatol (2001) 11:242–245

CASE REPORT

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A case of malignant fibrous histiocytoma on the knee joint in a patient with rheumatoid arthritis

Received: September 18, 2000 / Accepted: March 8, 2001

Abstract An elderly woman with rheumatoid arthritis and receiving nonsteroidal anti-inflammatory drugs (NSAIDs) treatment was diagnosed with a malignant fibrous histiocytoma in her left knee joint. However, no metastatic lesion caused by the malignant fibrous histiocytoma was found, probably owing to the NSAIDs therapy. Her general condition worsened, and eventually led to renal failure and death from progressive respiratory failure caused by pulmonary effusion. This is the first known report of a malignant fibrous histiocytoma originating in the left knee joint that was complicated by rheumatoid arthritis.

Key words Malignant fibrous histiocytoma · Rheumatoid arthritis

Introduction

Malignant fibrous histiocytoma (MFH) is a primitive sarcoma originating in deep soft tissue, and characterized by a dimorphic population of fibrocytic and histiocytic cells, usually arranged in a storiform pattern.[1–7] Approximately 30% of malignant fibrous histiocytomas occur in the lower extremities. The distal femur or proximal tibia are usually the sites affected, and the patella is rarely involved.[5] There has been interest in the association of MFH with various hematopoietic diseases,[1–6] but an association with rheumatoid arthritis (RA) has not previously been described.

In general, RA patients demonstrate an increased risk of hematopoietic diseases, and a decreased risk of stomach and rectal cancer.[8,9] This increased risk may be due to the persistent immune stimulation associated with RA itself, while the risk reduction for gastrointestinal cancer may be related to long-term nonsteroidal anti-inflammatory drugs (NSAIDs) treatment, which is common with these patients.[8,9] However, the risk of MFH in RA patients has not described been previously.

We present a case of malignant fibrous histiocytoma in the knee joint complicated by RA. The patella was completely destroyed by the MFH, and thus it may have originated there.

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Case report

In June 1998, a 77-year-old woman noticed pain in her left knee joint along with a slight swelling, which gradually increased. She was subsequently examined at a local hospital in September 1998. Her general condition worsened and a high fever developed, and she was therefore transferred to our hospital for diagnosis and treatment. Since 1971, from the age of 50, the patient had been suffering from RA, along with polyarthritis and morning stiffness, for which she was given NSAIDs treatment, but not disease-modifying antirheumatic drugs (DMARDs), and immune suppressive drugs. Her familial history revealed that her son also had RA.

On admission, her temperature was 40.9°C, her pulse was 122/min, her respiration was 36/min, and her blood pressure was 116/76 mmHg. The patient was alert and there were no neurological findings. A stethoscope examination revealed moist rales at both lung bases and a decreased breath sound at the left lung base. There were no abnormal findings for the heart or abdomen. Deformity or ankylosis resulting from the RA was observed at the bilateral joints, including the distal interphalangeal, proximal interphalangeal, metacarpophalangeal, wrist, elbow, shoulder, hip, knee, and ankle joints. In particular, her left shoulder joint demonstrated a narrowing of the joint space, deformity of the humeral head, and bone erosion in the humeral head (arrow) on X-ray (Fig. 1a). A 6.5 × 10-cm-diameter mass

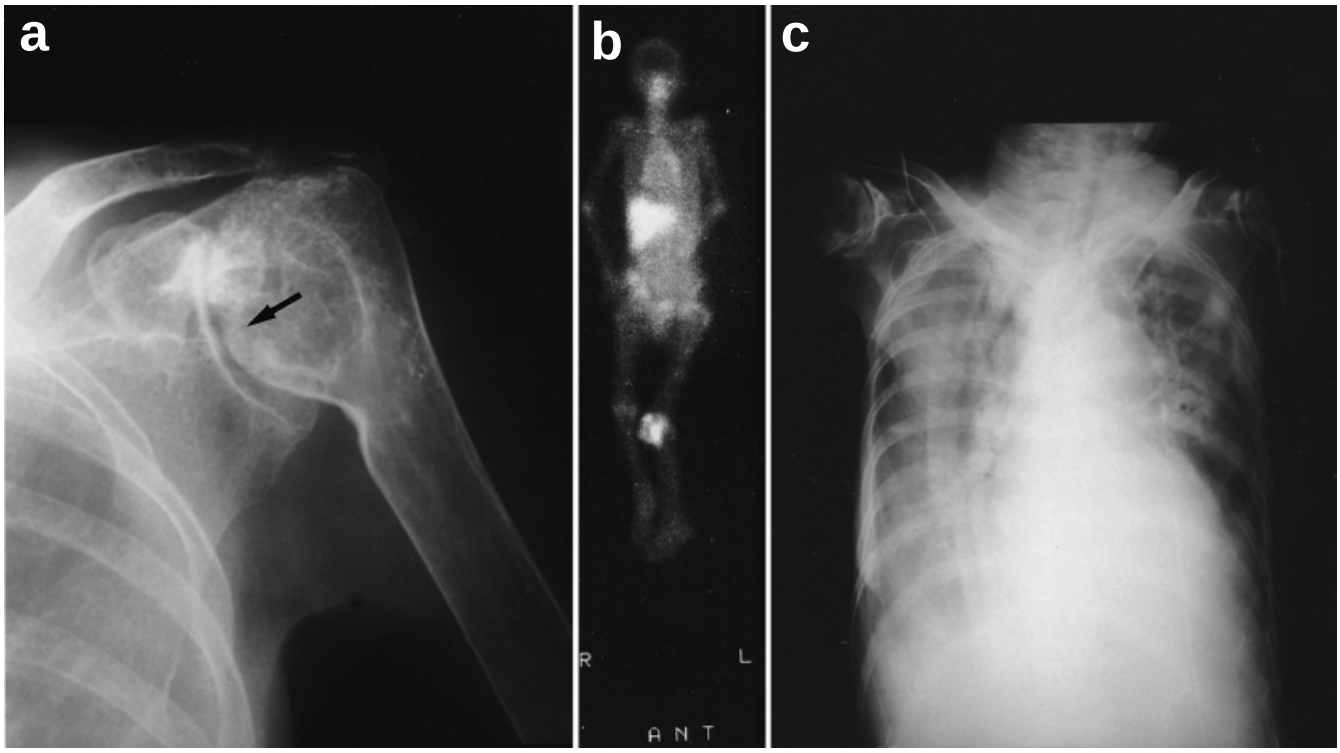

Fig. 1. a A roentgenogram of the patient's left shoulder, taken on admission, showing the narrowing of the joint space, deformity of humeral head, and bone erosion in the humeral head (*arrow*). **b** Gallium scintigram taken on admission; only the uptake in the left knee was revealed. **c** Chest roentgenogram taken on the day of death. A bilateral infiltrative shadow and pleural effusion can be recognized

Table 1. Laboratory findings on admission

Urinalysis		Blood chemistry		Serology		Blood coagulation	
Protein	(1+)	TP	6.9 g/dl	CRP	8.4 mg/dl	PT	53%
Sugar	(2+)	Alb	1.6 g/dl	ESR	94 mm/h	APTT	53.3 s
Occult blood	(1+)	T-Bil	1.0 mg/dl	IgG	3910 mg/dl	PIC	2.9 μg/ml
Sediments		D-Bil	0.5 mg/dl	RF	158.6 IU/ml	TAT	0.4 μg/ml
RBC	30–49/HPF	AST	4 IU/l	ANA	×40		
WBC	100/HPF	ALT	4 IU/l	Anti-ssDNA	10.1 AU/ml		
Epithel	1–4/HPF	ALP	265 U/l	Anti-dsDNA	9.0 IU/ml	Tumor marker	
No casts		LDH	169 U/l	Anti-RNP	Negative	Ferritin	912 mg/ml
		AMY	8 U/l	Anti-Sm	Negative		
Hematology		CK	6 U/l	Anti-SS-A	Negative		
WBC	14900/μl	T-CHO	89 mg/dl	Anti-SS-B	Negative		
St	9.0%	TG	106 mg/dl	Anti-Scl-70	Negative		
Seg	89.0%	BUN	6 mg/dl	Anti-Jo-1	Negative		
Lym	1.0%	UA	1.2 mg/dl	Anti-CL-β2GPI	Negative		
Mono	1.0%	Cr	0.41 mg/dl	RF-IgG	Negative		
Eosino	0.0%	Na	128 mEq/l	CH50	23.2 IU/ml		
Baso	0.9%	K	2.3 mEq/l	IC-C1q	3.4 μg/ml		
RBC	318×10^4/μl	Cl	96 mEq/l	IC-anti-C3d	29.4 μg/ml		
Hb	8.8 g/dl	Fe	18 μg/dl				
Ht	26.1%	Glu	142 mg/dl				
Plt	20.1×10^4/μl						

RBC, red blood cells; WBC, white blood cells; HPF, high-power field; Hb, hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; CK, creatine kinase; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IgG, immunoglobulin G; RF, rheumatoid factors; ANA, antinuclear antibodies; RNP, ribonucleoprotein; PT, prothrombin time; APTT, activated partial thromboplastin time

was palpable in the left patella (Fig. 2a), and a 15 × 9-cm-diameter decubitus ulcer was located behind it.

Laboratory data on admission are summarized in Table 1. Urinalysis results showed 2+ for sugar, 1+ for protein, and 1+ for occult blood, while the sediments contained 30–49 red cells, 100 white cells, and epithelial casts in the high-power field. Complete blood counts on admission showed leukocytosis (WBC 14900/μl) and anemia (RBC 318 ×

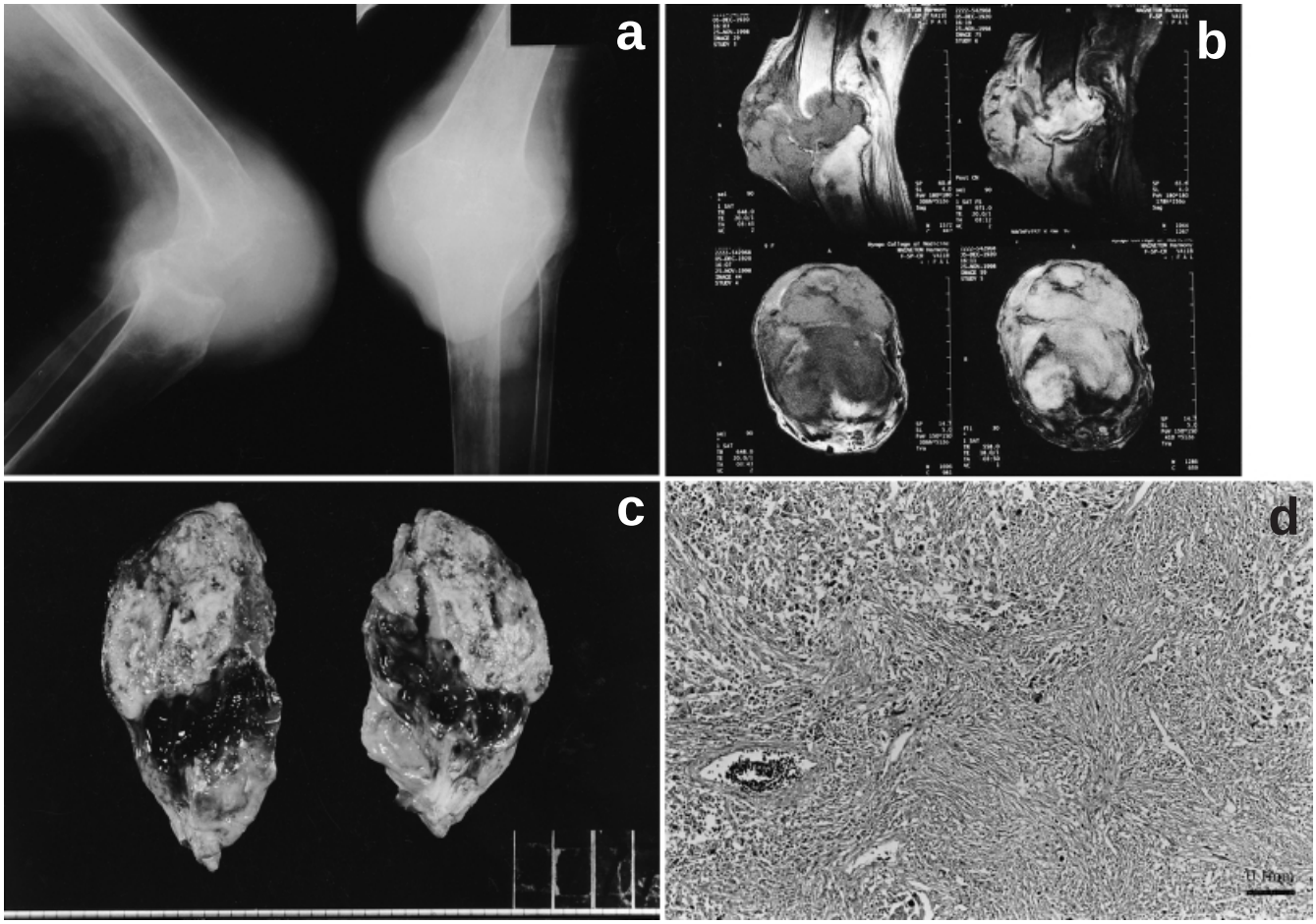

Fig. 2. **a** Roentgenogram of the left knee. **b** Magnetic resonance imaging (MRI) of the left knee on admission. A 6.5 cm × 10 cm mass shadow can be seen. This mass showed irregular low, signal intensities on T1-weighted images and a predominantly high-intensity area on T2-weighted images, and could be enhanced by gadolinium. **c** Left knee tumor at autopsy. **d** Histology of the tumor. An autopsy of the left knee joint revealed a storiform–pleomorphic type of malignant fibrous histiocytoma (hematoxylin–eosin staining)

10^4 μl, hemoglobin 8.8 g/dl). The erythrocyte sedimentation rate (ESR) was 94 mm/h, and C-reactive protein (8.9 mg/dl) was elevated. Blood chemistry analysis revealed marked hypoalbuminemia, hypocholesterolemia, hypotriglyceridemia, hyponatremia, and hypokalemia. The serological test was positive for rheumatoid factor (RF, 158.6 IU/ml, normal <0.6), but negative for antinuclear antibodies. The serum concentration of immunoglobulins (IgG, 3910 mg/dl) was extremely high, and complements (CH50:23.2 IU/ml) were extremely low. Circulating immune complex (C1q, 3.4 mg/ml <2.9; anti-C3D antibody, 29.4 mg/ml <9.2) was positive.

On magnetic resonance imaging (MRI), a 6.5 cm × 10 cm mass shadow was revealed in the patient's left knee. This mass showed irregular low signal intensities on T1-weighted images and a predominantly high-intensity area on T2 weighted images, and could be enhanced by gadolinium. Further, the invasive tumor lesion had caused osteolytic destruction of the distal end of the left femur, the top of the tibia, and the patella, and had also invaded the left popliteal artery (Fig. 2b). A histopathological examination of the left knee biopsy specimen showed a malignant fibrous histiocytoma. Only the uptake in the knee was shown on a gallium scintigram (Fig. 1b) at the first examination. On admission, the patient was also found to have sepsis (*Bacillus ovatus*), pneumonia, a urinary tract infection, and a decubitus ulcer in her hip area.

We considered amputation of the left leg to treat the tumor, but her general condition worsened, making surgery impossible. She eventually experienced renal failure and died of progressive respiratory failure caused by pulmonary effusion and congestion (Fig. 1c).

The autopsy findings showed a malignant fibrous histiocytoma in the left knee joint (Fig. 2c), although no metastatic lesion caused by the malignant fibrous histiocytoma was found. Microscopic findings of the tumor showed a storiform–pleomorphic type of malignant fibrous histiocytoma, with plump spindled cells arranged in short fascicles in a cartwheel or storiform pattern around inconspicuous slit-like vessels. Further, the cells were oriented in a random or haphazard fashion with respect to the blood vessels (Fig. 2d).

Discussion

Malignant fibrous histiocytoma (MFH) is a primitive sarcoma originating in the deep soft tissues, and characterized by a dimorphic population of fibrocytic and histiocytic cells, usually arranged in a storiform pattern. It is one of the most common soft-tissue sarcomas found in adults and is distinctly uncommon before the fourth decade of life, with a peak incidence in the seventh decade. The majority of these tumors occur in one of the extremities, the retroperitoneum, or the abdomen, with the thigh being the single most common site.[1–7] The present patient was 77 years old and the tumor was found in the left knee joint. It had probably originated primarily from the patella, although this had been completely destroyed by the lesion.

Seventy percent of malignant fibrous histiocytomas found in bone develop as primary tumors without a known predisposing cause, while 30% occur in bone which is affected by preexisting disease or radiation therapy.[1–6] These preexisting conditions include bone infarctions, Paget's disease, osteomyelitis, hereditary bone dysplasia, renal transplantation, caisson disease, chronic alcohol abuse, and sickle-cell traits. In the present case, the preexisting condition for the tumor originating in the knee joint was rheumatoid arthritis, which to our knowledge is the first example reported.

Histologically, the present tumor was diagnosed as a storiform–pleomorphic type of malignant fibrous histiocytoma. It was composed of spindle cells, predominantly arranged in a storiform pattern, and infiltrating bone, skeletal muscle, and adipose tissue. Necrotic areas, increased vascularity, and multinucleated giant cells were seen. There were moderate-to-marked nuclear pleomorphisms, with hyperchromasia and numerous mitotic figures (Fig. 2d).

In general, malignant fibrous histiocytoma metastatic lesions have been reported in the lungs (82%), lymph nodes (32%), liver (15%), and bone (15%).[1–5] On our first examination of the present patient, only uptake in her knee was revealed on a gallium scintigram. Autopsy findings revealed no metastatic lesion caused by the malignant fibrous histiocytoma.

In studies of RA, several doctors have noted an increased risk of myeloma with MFH, as well as a significantly increased risk of cancer in the respiratory organs in men, and a decreased risk of stomach and rectal cancer in women.[8,9] The increased risk of lymphoproliferative and myeloproliferative malignancies in RA may be related to the use of immune suppressive drugs (such as azathioprine, methotrexate, and cyclophosphamide).[10] Further, the lower risk of stomach and rectal cancer may be related to a long-term use of NSAIDs therapy in RA.[9] Notably, a selective COX-2 inhibitor class of therapeutic agents are used for colorectal cancer hematogenous metastases.[11,12] The present patient received only NSAIDs treatment, which suggests that NSAIDs suppress metastasis by the malignant fibrous histiocytoma. However, a risk of MFH in RA has not been reported, and the true incidence and biologic potential of this neoplasm have not been clearly determined.

In summary, the present case is a very rare occurrence of primary malignant fibrous histiocytoma in an RA patient, which probably originated in the patella.

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